Nutritional Anaemias

Uptodate: Clinical Nutrition

Presented by Dr Michael Rose, Department of Haematology, St George's Hospital Medical School.

University of London Audio-Visual Centre, 1977.

Produced by David Sharp.

Made for British Postgraduate Medical Federation.

Black and white
Duration: 00:28:03:12

00:00:00:00

<**Dr Michael Rose to camera**>

By definition, nutritional anaemias develop in states of inadequate nourishment.

<**Rose over table listing reasons for inadequate nourishment**>

Such inadequate nourishment will be related to dietary deprivation, to states where there is impaired intestinal absorption and may intermittently occur where a previously adequate balance is changed because of particular physiological requirements, such as those of pregnancy, childbirth and infancy.

<**Rose over still photographs of: carcass of a cow and undernourished African child; urban tower block and other scenes of urban poverty; a pile of nutritionally valuable food**>

There are states which develop particularly in rural environments, consequences of famine and of drought where the nutritional consequences are so gross that anaemia is, frankly, a relatively insignificant problem by contrast with the more pressing evident problems.

There are certain undeniable counterparts in urban societies. We are confronted with increasing evidence of urban decay and it's not difficult to understand the state of dismay and indifference amongst people who live under such circumstances; a feeling of impotence, insignificance and helplessness which prohibits their access to the wherewithal to look after themselves in either a responsible or circumspect manner.

Certainly, if this sort of food issued from the shopping basket, few of us would complain. And a person who ate this sort of food regularly would not be a candidate for nutritional anaemia. There is a sort of continuum of social deprivation leading from protein calorie malnutrition, where the nature of the anaemia almost defies description, to deficiencies of specific components in the diet such as iron, folic acid and vitamin B12.

<**Rose over table listing factors of dietary provision**>

If we consider the factors which influence the dietary provision to any one given individual, these can be classified into those which influence food and those variables affecting people.

If we consider food first: availability will fluctuate according to rainfall, according to farming habits; the cost will vary according to availability. The quality of food is going to differ in different parts of the world according to the content of the soil and rainfall. The variety of food is going to be changed according to the wealth of a particular community. Preparation of food will change, with changes in freezing, canning, packaging, and the presentation of food will differ amongst different cultural groups.

Let's now consider the variables which affect people. Clearly with increasing population density, there will be less food to go around and the wealth of any given group or family will determine what they are able to purchase. The access to food amongst dependants will be determined by the skills of the breadwinner and whether or not those skills are at high premium. There will be certain physiological stages such as childhood, infancy, pregnancy, old age, illness, convalescence which will determine the requirement for food in a given person. General health – anybody who sustains an illness of more than a few weeks duration will have some loss of appetite and, in due course, this is going to reflect because of the negative balance, or the deficient intake, of particular components of food for that duration. There'll be specific factors related to sanity, intellect and mobility – mobility in particular being determined by muscular skeletal disease, by neurological disease and so forth, which will determine whether they can go out and buy food, whether they know what food to buy, whether they are able to choose, whether they are able to prepare the food, whether they are able to actually sit down and eat the food with any joy at all.

00:05:42:20

<**Rose to camera**>

From what I've said, I hope it's clear that under optimum circumstances a balance is struck between nutritional intake and physiological requirements. That balance is struck so that nutritional intake should exceed the requirements. Clearly, at any given time, there will be differences in the mean daily / monthly intake of any given haematinic between one culture and another culture.

<**Rose over graph comparing haematinics of different cultures**>

Now, in respect of an unspecified haematinic, let's consider the condition in two different cultures with the mean daily intake identified on the line A and the line B. Now, if we consider a number of physiological life events in respect of requirements, and superimpose those, we can see that an individual from culture B, whilst okay for most of the time will go into negative balance, that's to say, their requirements

exceed provision, during infancy, during pregnancy and lactation, during an illness or convalescence. Whereas a subject from culture A will, throughout those physiological events, always have an excess of intake so that there will be no evidence of depletion.

<**Rose to camera, then over animated diagram looking at the effects of nutritional intake on folate, iron and B12**>

For the purposes of explaining the equilibrium, we suggested that the intake would be more or less constant. Now clearly there are instances where the constancy changes and the level of intake falls. Let's just consider what happens in respect of folate, iron and B12 when this intake changes.

Now, this is meant to represent the folate content of a body, marked in black. The rate at which folate is employed and used and degraded will be illustrated by the size of the arrows and the frequency with which they flash on and off. The events are such that folate gets used up and the subject will become depleted within a matter of weeks of stopping his folate intake. If we now consider the position in respect of iron. Iron is used up rather more slowly, the phenomena in which the iron is used up are entirely different but, nonetheless, if there is an obstacle to iron intake which starts from a given moment, iron depletion will develop within a matter of months. And finally, in respect to vitamin B12. Vitamin B12 is relatively stable; there is a colossal amount in the body by comparison with requirements, so that with an obstacle to intake, a total embargo, vitamin B12 depletion will only develop within a matter of 3 to 5 years.

<**Rose to camera, then over animated illustration detailing dietary absorption of iron**>

Now, I've spoken about the dietary content as if this really determines what is absorbed. But the position is a little bit more complicated than that with respect to the availability and in respect of deterioration on cooking.

Here we have an illustration which shows the lumen of the bowel, an interface and the portal blood. The iron content within the lumen will not all be absorbed, only a part will be absorbed and that part will be determined by certain regulatory mechanisms within the cells of the mucosa of the bowel – a proportion is absorbed, a proportion passes through the bowel unabsorbed. Now, few of us eat iron alone, it's generally within a complex of dietary constituents and under those circumstances, whatever the iron content, there are other determinants which influence the availability of that iron for absorption. This is particularly true in cereal foods and in bread, so that some of the iron becomes linked to so-called ligands which prohibit absorption, other parts of the iron become linked to other components which facilitate absorption. But in a balanced and varied diet, the iron available for that absorption is far less than it would be if the iron were ingested alone. The rest is passed through the lumen of the bowel, linked to these other dietary constituents, unabsorbed.

00:10:32:00

<**Rose to camera**>

So, if the major problem, in respect of iron availability is the presence of other dietary constituents interfering with iron absorption, in respect of folate, the problem is more closely related to cooking habits.

A vegetable placed in boiling water will lose upwards of 75% of its folate content within 3 minutes of immersion, thus the folate content of the proverbial landlady's cabbage is reduced to a minimum. The most effective dietary sources of folate are uncooked vegetables and salad. I'd like now to talk about iron.

The iron content of vegetables and food shows colossal variation according to climatic conditions, the constitution of the soil, rainfall and other variables which have yet to be defined. The iron contents of food may be natural, as in beans, lentils, vegetables in general. Or it may be artificial, an additive to flour and cereals. There's no doubt that on a global scale, iron depletion is the most important cause of nutritional anaemia. This probably comes as a surprise to people trained in Western

medical schools and with European medical experience, where the development of iron depletion tends to be synonymous with pathological blood loss. But on a worldwide scale there is no doubt that the most common cause of iron depletion is nutritional deficiency of that iron. This peaks in incidence at certain phases in life which, in a sense, are perfectly obvious. The peaks are in infancy and during pregnancy.

<**Rose over diagram and graph charting iron levels in a newborn during the 1st year of life**>

Now, let's consider the position in a newborn for the first year. The baby will pick up a certain load of iron from its mother and that represents a legacy with which it's stuck for the first 6 to 9 months of its life. As the baby grows, the blood volume will increase and effectively the baby is bleeding into its own expanding blood volume. Its extraneous sources of dietary iron are limited and, thus, if the baby is born with insufficient iron, it will proceed within those six months, almost predictably, into a state of iron deficiency.

This picture illustrates the events which take place vis-à-vis iron during pregnancy. As you can see, there is a gradual increase in the rate of transfer from mother to foetus during the first two thirds of pregnancy, then there's a change in the slope of the graph so that there's an accelerated transfer during the latter phase of pregnancy. Thus, if a baby is born prematurely, that will take place at the expense of a very considerable quantity of iron which never gets across because the gestation does not proceed to term.

<**Rose over graph charting iron levels in the early years of a young woman's life, then a table listing how iron inherited from mother to child may be insufficient**>

Now let's just consider the position in the early years of a woman's life. We reach a certain plateau of iron intake and then if we superimpose a number of the events that a normal growing female will encounter, they will represent changes in iron

requirement. Up to the ages of 11, 12, with the onset of menstruation, the requirements of iron are relatively trivial. Then there's a change, possibly a doubling of requirement, and with this apparently relatively adequate intake, this particular female will only exceed her intake once she becomes pregnant. Clearly, we have levelled off the intake line in a more or less random way and by just shifting the line downwards we could see a way to producing a much more chronic, enduring state of iron depletion. This iron depletion, or the iron requirement, is also continued through lactation and then will gradually fall again to the pre-existing level.

Thus, a newborn child will be particularly vulnerable to iron depletion during its first 6 months if there was any measure of prematurity; if there are multiple births because it's obvious that if there are lots of foetuses then there will be more foetuses to provide a unit amount of iron to; if the parents and siblings are malnourished even though the growing foetus is sustained at the expense of the mother, her resources may be exceeded and the baby is born with less iron than it should be; and then, after the baby's birth if the additional sources of dietary iron are even less than normal, as when provided in the form of goat's milk, then again the baby will be destined to the development of iron depletion. Such anaemia not only results in a failure to thrive but also may increase susceptibility to infection and has all sorts of other consequences.

00:16:42:00

<**Rose to camera, then over diagrams showing how folate is absorbed**>

There are also specific circumstances in which there is impairment of iron absorption. In particular, after partial gastrectomy, upwards of 80% of such subjects will develop iron deficiency within a period of 3 to 5 years after the operation. Also diffuse bowel disease, particularly affecting the duodenum, as in celiac syndrome, will result in impaired iron absorption.

I'd now like to turn to folic acid. The dietary sources of folic acid are, as I've suggested, mainly in green vegetables, but also in dairy produce, in fruit, in kidneys,

liver and in beer. The forms of folate are either as a so-called monoglutamate of pteroyl-L-glutamic acid, illustrated here – the glutamic acid residue is the extension towards the middle of the illustration, and as polyglutamates where there are a variety of additional glutamic acid residues, extending to the number of 7.

The absorbability of folic acid seems to be in some way related to the number of glutamic acid residues, thus monoglutamates are most easily absorbed and the polyglutamates require conversion into monoglutamates before absorption.

Here we have an illustration, the wavy line is the interface between the bowel lumen and the portal blood. The monoglutamate, at the top, moves directly across into the portal blood. The heptaglutamate, at the bottom, is converted, probably within the microvilli of the brush border of the small bowel cells, into monoglutamate before being absorbed.

<**Rose to camera**>

The identification of clinically important and overt folate depletion presupposes certain things. It presupposes that one has the personnel and apparatus and methods to identify its presence, and secondly, that the subjects concerned have sufficient protein intake and iron in their diets to preclude the development of more prominent and different conditions.

The major cause of folic depletion is dietary inadequacy. It may be that the diet is inherently insufficient in its folate content or that by the time an otherwise reasonable diet has been prepared and provided for eating that whatever folate it originally contained has been destroyed.

Folate depletion may develop as a concomitant of a variety of long-standing chronic conditions: insanity, idiocy and chronic ill-health which interferes with appetite over a long period.

<**Rose over series of still images showing a pregnant woman and then a baby**>

It may also develop, almost predictably, as an acute phenomenon at various stages in life. Pregnancy, as with iron, is a phase in which folate depletion is commonly identified, also infancy, because as the child grows, the cells proliferate and the resources of folate are used up in that process.

00:20:19:00

<**Rose to camera, briefly over still photograph of sickle cells, then back to camera**>

Although dietary deprivation is far and away the most important cause of folate deficiency, it may also develop as a result of perfuse small bowel disease where there is interference with the absorption of folate acid. This develops in such conditions as tuberculosis, lymphoma and coeliac disease.

If we can return to the concept of a balance between intake and requirement. The requirements sometimes exceed those which are normal by twofold, fivefold or even tenfold and this is best illustrated by certain haematological conditions.

Lifelong haemolytic states such as sickle cell disease, illustrated here with some sickle cells, hereditary spherocytosis and thalassaemia. In these conditions, the bone marrow activity exceeds normal, that is to say, the cell proliferation is maybe 10 times the normal level, and this uses up possibly 10 times the amount of folate, thus these subjects have far less latitude in respect of their folate stores and are candidates for a rapid depletion in total body folate in the event of any interference with their intake.

Now, let us finally talk about vitamin B12 which really gives us our simplest task.

<**Rose over illustration of cattle in a field, then to camera**>

The biological sources of vitamin B12 are exclusively in microorganisms. These microorganisms are present in the soil, they contaminate the vegetation; cattle,

poultry and domestic animals eat the vegetation, the vitamin B12 goes in inadvertently, is absorbed amongst these micro organisms and then is deposited within the tissues of these animals. The B12 is then transferred into certain products from the animals such as eggs from the chicken; milk, butter, cheese from the cow. There is also vitamin B12 present in the tissues of the animals so that when the meat is eaten vitamin B12, again, is available for the man eating it.

The distribution of vitamin B12 is so ubiquitous and vast and the stores are so colossal in relation to daily requirements that it is very difficult to visualise a circumstance in which a person could develop a nutritional depletion. In order to do so, one would really have to work at it. It would be insufficient just to become a secular vegetarian not eating meat and not eating fish. Nutritional depletion is, indeed, seen amongst certain religious groups where there is a prescription, not only on the eating of animal tissues but on the eating all animal produce. This is a sect amongst the Hindu, called vegans: they eat no meat, fish, drink no milk, no butter, no cheese. Their only sources of vitamin B12 are amongst the organisms which contaminate the vegetables which they eat and possibly also the infinitesimal quantities of B12 in the drinking water and the water that they use to prepare the vegetables.

00:24:00:00

<**Rose over plate of beans with capsules of cytamen**>

Nonetheless, as these subjects, originally from Asia, have become dispersed around the world and are certainly seen in the United Kingdom, the development of nutritional B12 depletion has become likewise widely dispersed. It possibly is worth mentioning that since the B12 depletion that these subjects develop is nutritional in origin, it is amenable to nutritional correction. This plate, for instance, of beans containing probably very, very little B12, could be replenished in respect of its B12 content by opening a capsule of Cytamen. And in such families where the dietary habits proscribe all animal tissues and animal produce, it is worth advising the cook

that deposition of some B12, maybe once a week in the family dish, would avoid the depletion of B12 amongst their family.

<**Rose briefly to camera, then over animated diagram showing first normal B12 absorption, then absorption in the case of pernicious anaemia**>

The other major nutritional cause of B12 depletion is pernicious anaemia. The events involved in normal B12 absorption are rather curious and probably familiar to most of you. Vitamin B12 enters the stomach and comes into close proximity with a glycoprotein produced by the gastric parietal cells in the mucosa. This intrinsic factor has a specific site for union with the vitamin B12 molecule, and this complex is then conveyed out of the stomach into the distal small bowel where the intrinsic factor mediates absorption of vitamin B12.

In pernicious anaemia, there are a number of changes. Firstly, the mucosa, which is illustrated around the outline of the stomach, becomes shrivelled. The B12 which gets into the gastric lumen may come into the proximity of some intrinsic factor, but auto antibodies, specifically related to the intrinsic factor, occlude the zone to which the B12 would otherwise become attached. Thus, the intrinsic factor and B12 remain independent and the B12 passes down into the bowel without the factor required to mediate its movement across the ileum.

<**Rose to camera**>

There are also a number of relatively rare conditions which cause vitamin B12 depletion, but these really fall outside the brief of this talk.

We've thus spanned a variety of causes of nutritional anaemia, extending from the outrages of famine and protein calorie malnutrition, more amenable to political solutions than medical. Iron depletion, worldwide probably the most common cause of nutritional anaemia, again, probably more amenable to the activities of organisation than of individual doctors. Folate depletion, a relatively common nutritional cause of anaemia in the United Kingdom and throughout the world. And

vitamin B12 depletion which is possibly the only condition which still falls within the province of conventional medical methods for diagnosis and treatment.

<**End credits**>